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L4             2 S L1 FULL

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L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:707131 CAPLUS
DOCUMENT NUMBER: 133:267154
TITLE: Preparation of nitrogen mustard compounds and prodrugs
INVENTOR(S): Springer, Caroline Joy; Davies, Lawrence Christopher
PATENT ASSIGNEE(S): Cancer Research Campaign Technology Limited, UK
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058271	A1	20001005	WO 2000-GB1194	20000329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 513759	A	20010928	NZ 2000-513759	20000329
EP 1165493	A1	20020102	EP 2000-918981	20000329
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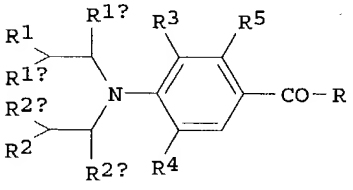
JP 2002540186	T2	20021126	JP 2000-607975	20000329

PRIORITY APPLN. INFO.: GB 1999-7414 A 19990331
WO 2000-GB1194 W 20000329
OTHER SOURCE(S): MARPAT 133:267154
GI

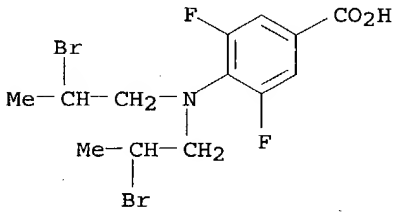


I

AB Nitrogen mustard compds. and prodrugs I [R = OH or NHCH(Z)CO2R7, resp., where R1, R2 = Cl, Br, I, OSO2Me, or OSO2Ph; R1a, R2a, R1b, R2b = H, C1-4-alkyl or -haloalkyl; R3 = F, Cl, Br, I, OCHF2, C.tplbond.CH, OCF3, Me, CF3, SF5, SCF3, or CF2CF3; R4 = H, any group given for R3; R5 = H, F; R7 = H, Me3C, allyl; Z = (un)substituted -CH2-T-W, where T = CH2, O, S, S(O), or SO2; W = CO2H, CONH2, SO2NH2, SO3H, PO3H2, tetrazol-5-yl, heterocyclylthio, etc. (with provisos)] were prepd. for use in therapy and treatment, for example, of cancer. Thus, [3,5-difluoro-4-[bis(2-iodoethyl)amino]benzoyl]-L-glutamic acid, prepd. via amidation of 3,5-difluoro-4-[bis(2-iodoethyl)amino]benzoic acid with di-tert-butyl-L-glutamate hydrochloride, showed antitumor activity against breast carcinoma in mice at 0.98 mM vs. 2.9 mM for the prior art compd. [3-fluoro-4-[bis(2-chloroethyl)amino]benzoyl]-L-glutamic acid.

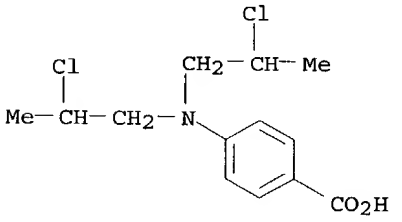
IT **298211-31-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of nitrogen mustard compds. and prodrugs)
RN 298211-31-1 CAPLUS
CN Benzoic acid, 4-[bis(2-bromopropyl)amino]-3,5-difluoro- (9CI) (CA INDEX NAME)



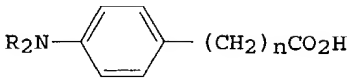
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1979:167816 CAPLUS
DOCUMENT NUMBER: 90:167816
TITLE: Some physicochemical properties and reactivity of p-[bis(2-chloroalkyl)amino]phenylalkanoic acids
AUTHOR(S): Karpavicius, K.; Juodvirsis, A.; Prasmickiene, G.; Knunyants, I. L.
CORPORATE SOURCE: Inst. Elementoorg. Soedin., Moscow, USSR
SOURCE: Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1979), (1), 51-8
CODEN: IASKA6; ISSN: 0002-3353
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB In p-(ClCHRCH2)2NC6H4(CH2)nCO2H (I; R = H, Me; n = 0-3) the cytotoxic amino groups exhibit an appreciable electron-donating effect, whereas the carboxyalkyl groups show a weaker effect. The CH2 protons in the amino group of I (R = H; n = 1-3) are magnetically equiv.; those in I (R = H; n = 0) and the analogous cinnamic acid derivs. are not. The hydrolysis of C-Cl in I appears to be 1st order; that of I (R = Me) is an order of magnitude faster than that of I (R = H).
IT **5379-46-4**
RL: PRP (Properties)
(NMR of)
RN 5379-46-4 CAPLUS
CN Benzoic acid, 4-[bis(2-chloropropyl)amino]- (9CI) (CA INDEX NAME)



L5 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1978:58444 CAPLUS
DOCUMENT NUMBER: 88:58444
TITLE: Physicochemical properties and antileukemia activity of some p-[bis(2-chloropropyl)amino]- and p-[bis(2-chloroethyl)amino]phenylalkanoic acid derivatives
AUTHOR(S): Karpavicius, K.; Prasmickiene, G.; Juodvirsis, A.; Ivanova, L. E.; Khomchenovskii, E. I.
CORPORATE SOURCE: Inst. Biokhim., Vilnius, USSR
SOURCE: Poiski Izuch. Protivoopukholevykh,

Protivovospalitel'nykh Mutagennykh Veshchestv (1977), 66-75. Editor(s): Kanopkaite, S. Akad. Nauk Lit. SSR, Inst. Biokhim.: Vilnius, USSR.
CODEN: 37BOA3
DOCUMENT TYPE: Conference
LANGUAGE: Russian
GI

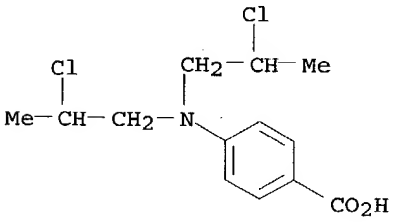


I

AB The rate of hydrolysis, pKa, PMR spectra, LD50, and antileukemic effects of 8 p-[bis(2-chloroalkyl)amino]phenylalknoic acids (I) were presented. The 2-chloropropyl derivs. had a greater reactive capacity than did the 2-chloroethyl derivs. owing to the presence of theelectron-donor Me group. The 2-chloropropyl derivs. were also generally more toxic than the 2-chloroethyl groups. The 2-chloropropyl derivs. were effective against granulocytopoiesis and on transplanted leukemias Nk/Ly and L-1210 in mice, whereas the 2-chloroethyl derivs. were effective against lymphopoiesis and development of Shchvetz leukemia in rats.

IT **5379-46-4**
RL: BIOL (Biological study)
(antileukemic activity and physicochem. properties of)

RN 5379-46-4 CAPLUS
CN Benzoic acid, 4-[bis(2-chloropropyl)amino]- (9CI) (CA INDEX NAME)



L5 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1978:15944 CAPLUS
DOCUMENT NUMBER: 88:15944
TITLE: Comparative study of the general toxicity and antileukemic activity of new phenylalkanoic acid derivatives under experimental conditions
AUTHOR(S): Ivanova, L. E.; Zaretskii, I. I.; Khomchenovskii, E. I.; Karpavicius, K.; Prasmickiens, G.
CORPORATE SOURCE: Moscow, USSR
SOURCE: Leikozologiya (1975), 4, 23-9
CODEN: LEIKDK
DOCUMENT TYPE: Journal
LANGUAGE: Russian
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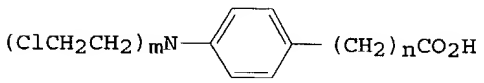


I

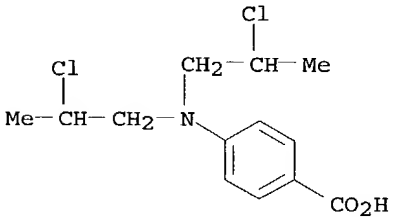
AB The toxicity and antileukemic effects of 8 phenylalkanoic acids (I) were detd. The 2-chloropropyl derivs., p-di(2-chloropropyl)aminobenzoic acid

[**5379-46-4**], p-di(2-dichloropropyl)aminophenylacetic acid [19521-09-6], p-di-(2-chloropropyl)aminophenylpropionic acid [22812-54-0], and p-di(2-chloropropyl) aminophenylbutyric acid [55774-31-7] had greater antileukemic effects than the resp. 2-chloroethyl derivs. although LD50 values tended to be lower.

IT **5379-46-4**
RL: BIOL (Biological study)
(leukemia inhibition by)

RN 5379-46-4 CAPLUS

CN Benzoic acid, 4-[bis(2-chloropropyl)amino]- (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1969:430178 CAPLUS

DOCUMENT NUMBER: 71:30178

TITLE: Synthesis and study of the reactivity of p-[bis(2-chloropropyl)amino]phenylalkanoic acids

AUTHOR(S): Prasmickiene, G.; Sukeliene, D.; Karpavicius, K.; Kil'disheva, O. V.

CORPORATE SOURCE: Nauch.-Issled. Inst. Onkol., Vilnius, USSR

SOURCE: Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya (1969), (3), 643-6
CODEN: IASKA6; ISSN: 0002-3353

DOCUMENT TYPE: Journal

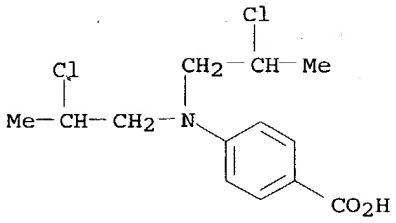
LANGUAGE: Russian

AB To 2.2 ml. POCl3 in Me2NCHO was added 5.72 g. p-(ClCHMeCH2)2NC6H4NH2 in the same solvent and the mixt. kept 1 day at 40.degree. to give p-(ClCH-MeCH2)2NC6H4CHO, (I), m. 104-6.degree.. I with N2H4 gave the appropriate ylidenehyrazine, m. 167-9.degree., while HONH2 gave the oxime, m. 125-7.degree., which after 3 hrs. reflux in Ac2O gave 71% p-(ClCHMeCH2)2NC6H4CN, m. 128-30.degree., which heated in concd. H2SO4 2 hrs. at 50.degree. gave the corresponding amide, m. 138-40.degree.. Oxidn. of the aldehyde or heating the benzamide with HCl gave p-(ClCHMeCH2)2NC6H4CO2H, m. 160-2.degree.. Propylene oxide added to p-H2NC6H4CH2CH2CONH2 in 30% AcOH gave, in 1 day, 77% (HOCHMeCH2)2NC6H4CH2CH2CONH2, m. 102-4.degree., which, heated with POCl3 1 hr., gave, on quenching in ice, 73% p-(ClCHMeCH2)2NC6H4CH2CH2CN (II), m. 66-8.degree., which in concd. H2SO4 2 hrs. at 50.degree. gave the corresponding amide, m. 58-60.degree.. I heated with malonic acid in pyridine-piperidine 3 hrs. gave 76% p-(ClCHMeCH2)2NC6H4CH:CHCO2H (III), m. 131-3.degree.. II heated with concd. HCl gave 59% corresponding free acid, m. 69-71.degree., also formed by hydrogenation of III over PdCaCO3.

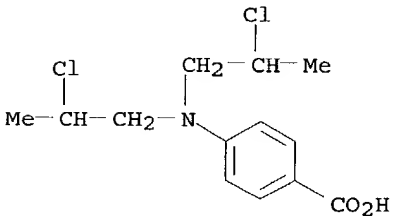
IT **5379-46-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 5379-46-4 CAPLUS

CN Benzoic acid, 4-[bis(2-chloropropyl)amino]- (9CI) (CA INDEX NAME)



L5 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1966:84288 CAPLUS
DOCUMENT NUMBER: 64:84288
ORIGINAL REFERENCE NO.: 64:15785d-g
TITLE: Tumor chemotherapy. XXX. Studies on the hexamethylenetetramine salt of p-bis(2-chloroethyl)amino-.omega.-bromoacetophenone
AUTHOR(S): Jen, Yun-Feng; Kao, I-Sheng
CORPORATE SOURCE: Inst. Mater. Med., Acad. Sinica, Shanghai, Peop. Rep. China
SOURCE: Huaxue Xuebao (1965), 31(6), 486-92,500
CODEN: HHHPA4; ISSN: 0567-7351
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB cf. CA 63, 17000b. p-(XRCHCH2)2NC6H4COCH2[(CH2)6N4]+Br- (Ia) (X = Br, R = H) (I), (X = I, R = H) (II), p-EtO2CNHC6H4COCH2[(CH2)6N4]+Br- (III), and p-EtO2CNHC6H4COCH2SC(:NH2+Br-)NH2 (IV), the analogs of the antitumor compd. AT-584, were prepd. The starting materials for the synthesis of I and II were p-bis[2-haloethyl (and propyl)] aminobenzoic acids (V and VI), resp. VI was synthesized by 2 methods: (1) [R(HO)CHCH2]2NC6H4CO2Et-p was first halogenated with PBr3 or POCl3 and then hydrolyzed with HCl or HBr to yield p-bis[2-chloropropyl (and 2-bromoethyl)] aminobenzoic acids. (2) Chlorination of p-bis(2-hydroxypropyl)aminobenzene with POCl3 in dimethylformamide gave p-bis(2-chloropropyl)aminobenzaldehyde, which was treated with KMnO4 in acetone to afford VI. The 2nd route gave a better yield. V and VI in benzene reacted sep. with SOCl2 to give the acid chlorides, which were treated sep. with diazomethane to yield the diazoacetophenones (VII). VII were decompd. in dioxane with HBr to form bromoacetophenone derivs., which treated with hexamethylenetetramine in chloroform gave I and II, resp. p-Aminoacetophenone was treated with ethyl chloroformate in the presence of triethylamine as the condensing agent to form p-ethoxycarbonyliminoacetophenone (VIII). When N,N-diethylaniline was used as the condensing agent instead of triethylamine, the yield was better. VIII was first brominated in acetic acid with Br and then treated with hexamethylenetetramine or thiourea to afford III and IV, resp. Preliminary pharmacol. examns. showed that I and II were as active as AT-584 against HeLa cells in culture medium, while III and IV were less active.
IT **5379-46-4**, Benzoic acid, p-[bis(2-chloropropyl)amino]- (prepn. of)
RN 5379-46-4 CAPLUS
CN Benzoic acid, 4-[bis(2-chloropropyl)amino]- (9CI) (CA INDEX NAME)



L5 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2004 ACS on STN

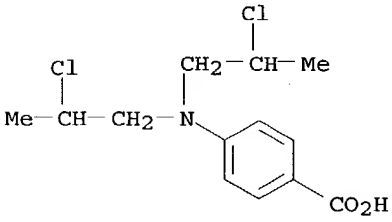
ACCESSION NUMBER: 1951:863 CAPLUS
DOCUMENT NUMBER: 45:863
ORIGINAL REFERENCE NO.: 45:139h-i,140a-g
TITLE: Aryl-2-haloalkylamines. VII. Some derivatives of 2-naphthyldi(2-haloalkylamines)
AUTHOR(S): Davis, W.; Everett, J. L.; Ross, W. C. J.
CORPORATE SOURCE: Roy. Cancer Hosp., London
SOURCE: Journal of the Chemical Society, Abstracts (1950) 1331-7
CODEN: JCSAAZ; ISSN: 0590-9791
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 44, 6838i. This work is a continuation of that in C.A. 43, 7442g, and 44, 1431e, in which it was shown that many arylbis(2-haloalkyl)amines inhibited the growth of various animal tumors and of spontaneous and transmitted leukemia in the Furth AK 1 pure line; 2-C10H7N(CH2CH2Cl)2 has been used clinically for the treatment of various lymphadenopathies in human patients with encouraging results. 1,7-AcC10H6NH2 (16 g.), added to 11.2 g. NaOH and 18.4 g. 50% N2H4.H2O in 175 g. (HOC2H4)2O and heated 3 hrs. at 195.degree., gives 14.5 g. 1,7-EtC10H6NH2, brown oil (Ac deriv., m. 167.degree.). 1,2,3,4-Tetrahydronaphthalene (264 g.), nitrated according to Schroeter (C.A. 16, 1673), gives 60 g. 5-NO2 and 45 g. 6-NO2 derivs.; catalytic reduction (Raney Ni) gives 5,6,7,8-tetrahydro-1- and -2-naphthylamines. 1-Keto-1,2,3,4-tetrahydronaphthalene oxime, reduced with Na in EtOH, gives 1,2,3,4-tetrahydro-1-naphthylamine, b10 114.degree.. These amines were converted into the N,N-bis(2-hydroxyethyl) derivs. in the usual manner but it is preferable to use SOCl2 in CHCl3 for the chlorination stage, N,N-Bis(2-chloroethyl)-2-methyl-1-naphthylamine, oil. 1,2,3,4-Tetrahydro-N,N-bis(2-hydroxyethyl)-1-naphthylamine, m. 89.degree. (picrate, m. 140.degree.); N,N-bis-(2-chloroethyl)-1,2,3,4-tetrahydro-1-naphthylamine-HCl, m. 158.degree.. 5,6,7,8-Tetrahydro-N,N-bis(2-hydroxyethyl)-1-naphthylamine picrate, m. 199.degree. (decompn.); N,N-bis(2-chloroethyl)-5,6,7,8-tetrahydro-1-naphthylamine, an oil (picrate, m. 121.degree.). N-(2-Naphthyl)-N-methyl-2-hydroxyethylamine picrate, m. 160.degree.; N-(2-naphthyl)-N-methyl-2-chloroethylamine, m. 52.5.degree. (inactive); N-(2-naphthyl)-N-methyl-2-hydroxypropylamine picrate, m. 154.degree.; N-(2-naphthyl)-N-methyl-2-chloropropylamine, m. 64.degree. (inactive). N,N-bis(2-hydroxyethyl)-6-methyl-2-naphthylamine, m. 94.degree.; N,N-bis(2-chloroethyl)-6-methyl-2-naphthylamine, m. 65.degree.; bis(2-bromoethyl) analog, m. 88.degree.; bis(2-iodoethyl) analog, m. 100-1.degree.. N,N-Bis(2-chloroethyl)-8-methyl-2-naphthylamine, m. 63.degree.; 8-Et homolog, m. 48.degree.; bis(2-bromoethyl)-8-ethyl analog, m. 57.degree.; bis(2-iodoethyl) analog, m. 85.degree.. 8-Acetyl-N,N-bis(2-hydroxyethyl)-2-naphthylamine, yellow, m. 113.degree.; bis(2-chloroethyl) analog, yellow, m. 84.degree.; bis(2-bromoethyl) analog, yellow, m. 94.5.degree. (solns. of the last 2 compds. exhibit an intense yellow-green fluorescence). N-(2-Chloroethyl)-1,2,3,4-tetrahydro-2-naphthylamine-HCl, m. 215.degree.; picrate, m. 197.degree.. N,N-Bis(2-chloroethyl)-1,2,3,4-tetrahydro-2-naphthylamine-HCl, m. 164.degree.; bis(2-bromoethyl) analog-HBr, m. 229.degree.. 5,6,7,8-Tetrahydro-N,N-bis(2-hydroxyethyl)-2-naphthylamine, m. 57.degree.; bis(2-chloroethyl) analog, m. 65.degree., photoluminescent. N,N-Bis(2-hydroxyethyl)-2-phenanthrylamine, m. 155.degree.; bis-(2-chloroethyl) analog, m. 91-2.degree.; bis(2-bromoethyl) analog, m. 111-12.degree.; bis(2-iodoethyl) analog, m. 117.degree.. N,N-Bis(2-hydroxyethyl)-3-phenanthrylamine, m. 109-10.degree.; bis(2-chloroethyl) analog, m. 73.degree.; bis(2-bromoethyl) analog, m. 98.degree.; bis(2-iodoethyl) analog, m. 125.degree.. 2-(2-Hydroxyethylamino)fluorene, yellow, m. 150.degree. (cf. C.A. 43, 7442g); 2-chloroethyl analog, m. 127.degree.. 2-[Bis(2-bromoethyl)amino]fluorene m. 137.degree.. N'-Propionyl-N,N-bis(2-chloroethyl)-p-phenylenediamine m. 101-3.degree.. p-[Bis(2-chloropropyl)amino]benzoic acid, m. 165-6.degree.; Me ester, m. 61.degree.. p-MeOC6H4N(CH2CH2Cl)2 (2.5 g.) and 3.4 g. Et2NCS2Na in 200 ml. 50% aq. Me2CO, refluxed 2 hrs., give N,N-bis[2-(diethyldithiocarbamyl)ethyl]-p-anisidine, m. 85-6.degree.. p-MeOC6H4[NCH2CH(OH)CH2Cl]2 (40 g.) in 500 ml. boiling ether, gradually treated with 40 g. KOH, gives N,N-bis(2,3-epoxypropyl)-p-anisidine, yellow, b9 228-9.degree.; this is inactive. Data are given for the rate

of hydrolysis of a no. of these compds. in 50% aq. Me2CO at 66.degree.. The effect of various substituents is discussed. There is the expected increase in the rate of hydrolysis on passing from the Cl to Br compd. but a somewhat surprising decrease for the iodides.

IT **5379-46-4**, Benzoic acid, p-[bis(2-chloropropyl)amino]- (prepn. of)

RN 5379-46-4 CAPLUS

CN Benzoic acid, 4-[bis(2-chloropropyl)amino]- (9CI) (CA INDEX NAME)



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     FILE 'REGISTRY' ENTERED AT 15:42:16 ON 15 JAN 2004
L2              0 S L1

     FILE 'CAPLUS' ENTERED AT 15:42:17 ON 15 JAN 2004
L3              0 S L2
                  S L1

     FILE 'REGISTRY' ENTERED AT 15:42:39 ON 15 JAN 2004
L4              2 S L1 FULL

     FILE 'CAPLUS' ENTERED AT 15:42:40 ON 15 JAN 2004
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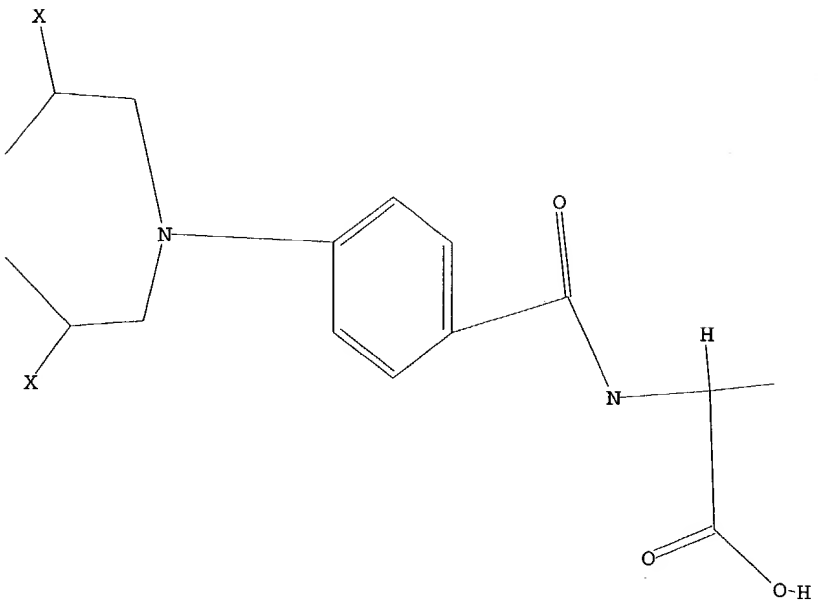

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Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

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100.0% PROCESSED 2 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 2 TO 124
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

L3 0 L2

=> s l1 full
REGlstRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

FULL SEARCH INITIATED 10:55:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 40 TO ITERATE

100.0% PROCESSED 40 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.02

L4 1 SEA SSS FUL L1

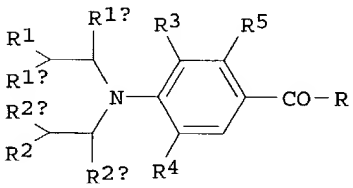
L5 1 L4

=> d ibib abs hitstr

L5 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:707131 CAPLUS
DOCUMENT NUMBER: 133:267154
TITLE: Preparation of nitrogen mustard compounds and prodrugs
INVENTOR(S): Springer, Caroline Joy; Davies, Lawrence Christopher
PATENT ASSIGNEE(S): Cancer Research Campaign Technology Limited, UK
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058271	A1	20001005	WO 2000-GB1194	20000329
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
NZ 513759	A	20010928	NZ 2000-513759	20000329
EP 1165493	A1	20020102	EP 2000-918981	20000329
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002540186	T2	20021126	JP 2000-607975	20000329

PRIORITY APPLN. INFO.: GB 1999-7414 A 19990331
WO 2000-GB1194 W 20000329
OTHER SOURCE(S): MARPAT 133:267154
GI



I

AB Nitrogen mustard compds. and prodrugs I [R = OH or NHCH(Z)CO2R7, resp., where R1, R2 = Cl, Br, I, OSO2Me, or OSO2Ph; R1a, R2a, R1b, R2b = H,

C1-4-alkyl or -haloalkyl; R3 = F, Cl, Br, I, OCHF2, C.tplbond.CH, OCF3, Me, CF3, SF5, SCF3, or CF2CF3; R4 = H, any group given for R3; R5 = H, F; R7 = H, Me3C, allyl; Z = (un)substituted -CH2-T-W, where T = CH2, O, S, S(O), or SO2; W = CO2H, CONH2, SO2NH2, SO3H, PO3H2, tetrazol-5-yl, heterocyclylthio, etc. (with provisos)] were prepd. for use in therapy and treatment, for example, of cancer. Thus, [3,5-difluoro-4-[bis(2-iodoethyl)amino]benzoyl]-L-glutamic acid, prepd. via amidation of 3,5-difluoro-4-[bis(2-iodoethyl)amino]benzoic acid with di-tert-butyl-L-glutamate hydrochloride, showed antitumor activity against breast carcinoma in mice at 0.98 mM vs. 2.9 mM for the prior art compd. [3-fluoro-4-[bis(2-chloroethyl)amino]benzoyl]-L-glutamic acid.

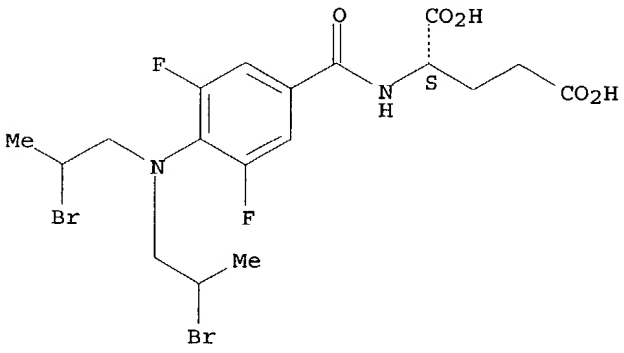
IT **298211-06-0P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of nitrogen mustard compds. and prodrugs)

RN 298211-06-0 CAPLUS

CN L-Glutamic acid, N-[4-[bis(2-bromopropyl)amino]-3,5-difluorobenzoyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Figure 1A

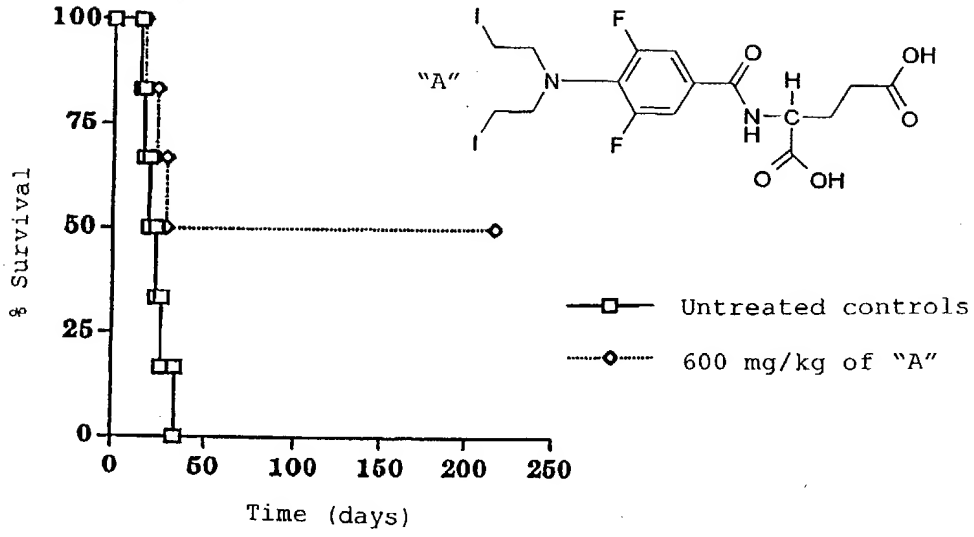

Figure 1B